REMARKS

The Applicants request reconsideration of the rejection. Claims 20, 21, 24, 29, and 33-36 are now pending.

The claims have been amended to ensure conformity with 35 U.S.C. § 112, first and second paragraphs, with an eye to the Examiner's comments found on pages 2-5 of the Office Action. However, the Applicants request reconsideration, or at least clarification, of the Examiner's determination that the specification is only enabling for methods of recovering nucleic acids from a nucleic acid-bearing material "requiring six steps as set forth from page 6, line 5 from the bottom, to page 9, line 6". Office Action at page 3, lines 4-6. The passage noted by the Examiner addresses features of the invention ranging from analysis of prior art problems to details of alternative preferred embodiments. The passage makes clear that certain of the "six steps" are optional or belong to subembodiments. The Applicants submit that each of the rejected claims, and each pending claim, is drafted with sufficient limitations to describe an embodiment of the invention that is distinguishable from the prior art.

Concerning page 5, lines 17-22, "nucleic acid-binding solid phase" refers to a solid phase to which a nucleic acid is bound. Using the former version of claim 33 as an example,

the recited step includes stirring the mixture containing the released nucleic acid, chaotropic agent, and substance at room temperature, with the result being a solid phase to which the released nucleic acid is bound. Therefore, former claim 33, for example, is consistent with the former version of independent claim 20 from which it is derived, because former claim 20 recites the step of contacting and mixing the solution containing the released nucleic acids and the chaotropic agent with the substance containing silicon oxide to bind the nucleic acids to the substance, and former claim 33 requires that the step include stirring the mixture, as well as providing a label for the substance to which the nucleic acid is bound.

The claims were rejected under 35 U.S.C. § 103(a) as being unpatentable over Boom et al U.S. Patent No. 5,234,809 in view of Seligson et al U.S. Patent No. 4,935,342. The Applicants traverse as follows.

Amended claim 20 now more particularly points out a step for mixing a nucleic acid-containing material with an accelerator substance containing a chaotropic substance for the binding of nucleic acids to a solid phase containing silicon oxide, and a step for contacted the mixture obtained in the mixing step to the solid phase containing silicon

oxide. In other words, the mixture is prepared before the mixture is contacted with the solid phase containing the silicon oxide.

In contrast, Boom requires, in each disclosed embodiment, that the nucleic acid-containing material, chaotropic substance, and silica particles be combined, with no teaching or suggestion that the nucleic acid-containing material and chaotropic substance be first mixed, followed by contacting the mixture to the silica particles. Note, for example, column 2, lines 13-18 ("These objects are realized according to the invention by a process... characterized by mixing the starting material with a chaotropic substance and a nucleic acid binding solid phase"); and column 4, lines 3-12 "The process according to the invention will usually be carried out in such a way that the starting material is mixed with sufficiently large amounts of chaotropic substance for instance guanidinium salt and for instance silica particles to release essentially all of the nucleic acid present in the starting material and bind it to said silica particles. A suitable protocol, is, e.g., the addition of a suspension of silica particles to a buffered GuSCN solution present in a reaction vessel, followed by addition of the sample and thoroughly mixing" (emphasis added).

Seligson was applied as teaching a step, no longer present in the independent claims, of releasing the nucleic acid from the nucleic acid-bearing material and forming an aqueous solution containing the released nucleic acid, prior to adding the chaotropic agent and binding the nucleic acid to the substance containing silicon oxide. Thus, although the application of Seligson is no longer an issue for this feature, the Applicants traverse the Examiner's supporting the addition of Seligson to the teachings of Boom in an attempt to show that the person of ordinary skill would deem it obvious to digress from Boom's requirement that the starting material and chaotropic substance be mixed in the presence of the solid phase "since Boom at al disclosed that starting material cells may be subjected to lysis (col 2, line 45), and since it would have been expected that nucleic acids bound within cells will [be] unavailable for adsorbing to the solid phase of Boom et al." Office Action at page 7, lines 13-16. The Applicants note that this lysis according to Boom takes place before the performance of Boom's method: "Therefore, such starting materials require a pretreatment rendering the cells accessible, e.g., a preceding cell lysis after which the resulting lysate can be subjected to the process according to the invention." (Emphasis added) column 2, lines 43-46. In

other words, after the lysis, Boom teaches to mix the sample with the chaotropic substance and silica particles, such that the simultaneous combination of these three materials is not changed by the lysis mentioned by the Examiner.

Further, the Examiner asserts that it would have been obvious to add the chaotropic substance to the aqueous solution of nucleic acid of Boom before adding the aqueous solution to the solid phase "since Boom et al combines the chaotropic substance, starting material and solid phase together so released nucleic acids will immediately bind to the sold phase." This statement, however, uses Boom's teaching to allege its opposite. The person of ordinary skill is taught to make the combination at once, or to add the chaotropic substance to the solid phase before adding the sample; it is unsupportable to state that this teaching suggests not to do so.

Further, the Examiner is of the opinion that combining the three materials, according to Boom, brings an advantage (that the released nucleic acids will immediately bind to the solid phase; page 7, lines 20-21 of the Office Action). However, the inventors have found that creating the mixture prior to adding the mixture of sample and chaotropic substance to the solid phase beings advantages over the Boom

combination. Note the present specification at page 4, lines 4-16, in which a method similar to Boom's taught in JP 2-289596, requires a procedure for removing the guanidinium salt from the solid phase while retaining the nucleic acids bound to the solid phase, in order to obtain purified nucleic acids, although a suitable removing procedure is not described. That the "advantage" cited by the Examiner is further improved by the present invention is strong evidence of nonobviousness.

Furthermore, an advantage of the present invention not taught by Boom or Seligson is the two-step washing procedure of washing the solid phase binding the nucleic acids with a solution containing a chaotropic substance, and washing the solid phase with a solution containing alcohol and acetate. Boom teaches the known method of successive washings using a chaotropic substance, ethanol and acetone. Washing with ethanol and/or acetone, however, requires a procedure of removing the acetone by drying. Further, both ethanol and acetone are volatile, such that the procedure requires an apparatus having a highly airtight chamber and a close-open mechanism of a lid and/or a cooling mechanism for preventing volatilization of the reagents. Specification at page 4, line 26 thorough page 5, line 5. The two-step procedure of the claims gives the advantages of washing with the chaotropic

substance, in combination with advantages of washing with a solution containing both an alcohol and acetate, without the attendant problems of the prior art.

In this regard, the Applicants note the Examiner's comment on page 8, lines 2-7, that washing with acetate would be obvious because acetate "is a well known buffer component", and because Boom teaches washing with a washing buffer at column 4, line 22. However, the washing buffer of Boom is used in a washing step corresponding to the first of the claimed washing substeps (that is, the substep of washing with the chaotropic substance). Thus, to wash with acetate as the washing buffer, as alleged by the Examiner, would result in a washing procedure in which acetate is first used, followed by washing with ethanol and then acetone. Clearly, this substitution would not meet the limitations of the claims.

In addition, to the extent that acetate is so well known in a washing solution, the record would be better served were a reference teaching the use of acetate in the solution be applied as alleged by the Examiner.

It is noted that Seligson has been applied as teaching the use of a chloride salt in the washing. Of course, this limitation no longer forms part of the claimed invention. However, it is worth noting that the nucleic coupling form of

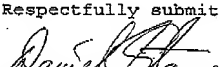
Boom is so different from that of Seligson that the person of ordinary skill would not apply the teachings of Seligson to those of Boom in order to meet the claimed washing, in any event. In particular, according to Boom, only the silicon oxide and the material housing the silicon oxide represent a solid phase for binding with the nucleic acids. On the other hand, Seligson teaches a material employing anion exchange as the solid phase. Silicon oxide, of course, does not have an anion exchange ability. Therefore, the conditions of extraction and elution of Boom are quite different from those of Seligson, and the kinds of salt useful in the washing solutions are quite different between the two methods. Specifically, the absorption process according to Boom is executed at a high density of salt, whereas the elution process is executed at a low density of salt. On the other hand, according to Seligson, the absorption process is executed at a low density of salt, and the elution of process at a high density of salt. Therefore, the person of ordinary skill would not deem it obvious to use the washing method from an anion exchange column according to Seligson for the purpose of recovering nucleic acids from a silicon oxide solid phase, using a chaotropic salt, as required by Boom. Misapplying the washing salt may result in an ineffective elution or the

presence of salt in the final eluted product, which could exert a negative influence in, for example, the composition of cell-free protein, reverse transcription reaction, or the like.

For each of the above reasons, the Applicants submit that the amended claims patentably define over both Boom and Seligson, whether taken individually, or in any combination. Further, the Applicants submit that Boom and Seligson are not properly combinable as set forth in the Office Action.

In view of the foregoing amendments and remarks, the Applicants request reconsideration of the rejection and allowance of the claims.

Respectfully submitted,



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